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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/900,963	07/10/2001	Claudine Guerin-Marchand	010830-118	8667

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EXAMINER	
LUCAS, ZACHARIAH	
ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 10/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/900,963	GUERIN-MARCHAND ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27-37* is/are pending in the application.

4a) Of the above claim(s) *28-30,34 and 36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27,31-33,35 and 37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 08/098,327.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 2-7-02.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Claims 27-37 are pending in the application.

2. Applicant's election with traverse of Group II, and the species represented by SEQ ID NO: 2 wherein X1 is Ser, X2 is Glu, X3 is Arg, and X4 is Glu, in the reply filed on September 6, 2006 is acknowledged. The traversal is on the ground(s) that there would be no undue burden on the Office for the examination of each of the claimed inventions, and that the Applicant is entitled to at least 10 nucleotide sequences. This is not found persuasive because the number of sequences in the application is large, each sequence requires a separate sequence and text search.

With respect to Applicant's reference to the MPEP, it is noted that the MPEP indicates that the Office will examine "up to ten sequences." It is currently the practice of the Office to permit one sequence per application. It is additionally noted that in the present case, the claims already require the search of multiple sequences (reading on a combination of SEQ ID NO: 2 and 38). Thus, in the present case, there is already additional burden on the Office.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 28-30, 34, and 36 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions or species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on September 6, 2006.

4. Claims 27, 31-33, 35, and 37 are under consideration.

Information Disclosure Statement

5. The information disclosure statement (IDS) submitted on February 7, 2002 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Specification

6. The substitute specification filed September 6, 2006 has not been entered because it does not conform to 37 CFR 1.125(b) and (c) because: the specification does not properly show all changes made to the specification compared to the previously pending version. In particular, the marked up copy does not accurately show the change in format of the provision of SEQ ID NOs for the primers on page 14 of the application as filed (page 18 of the submitted substitute specification).

Also, the marked up copy does not show the changes made to the first sequence presented on page 9 of the submitted substitute specification (the substitution of an E for a D previously in the sequence).

Additionally, it is not clear where support may be found for the changes being made to the sequences in Figures 1 and 3, or on page 9 (above). Applicant is requested to either point out where such support may be found in the application as filed, or to not include the New matter in the next submitted substitute specification.

Moreover, because the substitute specification has not been entered, the application also fails to comply with the sequence rules for the reasons set forth in the prior letters of August 21, 2006, and of May 9, 2006 (the Restriction Requirement).

7. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: DNA sequences encoding peptide sequences specific for the hepatic stages of P. falciparum bearing epitopes capable of stimulating the T lymphocytes

It is also suggested that the abstract of the application be amended to indicate the invention is drawn to DNA sequences encoding the peptides described therein.

Claim Objections

8. Claim 31 is objected to because of the following informalities: this claim refers to a DNA encoding the amino acid sequence of Figure 7. Section 2173.05(s) of the MPEP states 'Where possible, claims are to be complete in themselves. Incorporation by reference to a specific figure or table "is permitted only in exceptional circumstances where there is no practical way to define the invention in words and where it is more concise to incorporate by reference than duplicating a drawing or table into the claim.' In the present case, the claims may just as easily refer only to the amino acid sequence of SEQ ID NO: 38. The claim is therefore objected for reference to the indicated Figure.

Appropriate correction is required.

Claim Rejections - 35 USC § 101

9. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

10. Claims 27, 31, 32, 35, and 37 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. These claims are drawn to a nucleic acid encoding a *P. falciparum* liver-specific antigen (LSA) polypeptide comprising T-cell or T- and B- cell epitopes. Such nucleic acids would include the gene for LSA found in *P. falciparum* cells. The claims therefore read on naturally occurring compounds, and therefore on non-statutory subject matter.

It is suggested that the claims be amended to read on "isolated" DNA sequences.

Claim Rejections - 35 USC § 112

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 31-33 and 37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Each of claims 31-33 refers to particular sequence identifiers. However, the identifiers are separated from the remaining claim text by parenthesis. It is not clear what the use of the parenthetical marks is intended to indicate. It is suggested that the claims be amended to remove the parenthesis surrounding the sequence identifiers.

13. Claims 32, 33, and 37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Each of these claims reads on a DNA encoding the first 153 amino acids of SEQ ID NO: 37. SEQ ID NO: 37 is a DNA sequence. It is therefore not clear what amino acid sequence is being encoding by the claimed DNA.

As SEQ ID NO: 38 represents the sequence encoded by the DNA of SEQ ID NO: 37, the claim will be treated for the purposes of this action as though it reads on a DNA encoding SEQ ID NO: 38.

14. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

15. Claims 27, 32, 35, and 37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 27, 35, and 37 are drawn to a genus of DNA molecules that encode polypeptides comprising at least one T-cell epitope, and optionally additionally encode a B-cell epitope, from the liver-stage specific (LSA) protein of *P. falciparum*. Thus, the claims are drawn to a genus of DNA molecules identified by the function (epitopes) of the polypeptides that they encode. Claim 32 is drawn to a DNA encoding residues 1-153 of SEQ ID NO: 38 or "an epitope

effective portion thereof." This claim is therefore drawn to DNAs encoding the polypeptide of residues 1-153 of SEQ ID NO: 38, or any fragment thereof comprising an epitope.

The following quotation from section 2163 of the Manual of Patent Examination Procedure is a brief discussion of what is required in a specification to satisfy the 35 U.S.C. 112 written description requirement for a generic claim covering several distinct inventions:

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice..., reduction to drawings..., or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus... See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406.
>
> A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

Thus, when a claim covers a genus of inventions, the specification must provide written description support for the entire scope of the genus. Support for a genus is generally found where the applicant has provided a number of examples sufficient so that one in the art would recognize from the specification the scope of what is being claimed.

In the present case, the application has not disclosed any specific T- or B-cell epitopes from the LSA protein. The application does indicate that T-cell epitopes may be found in each of the sequence repeats found in the first 153 amino acids of the LSA protein, and that B-cell epitopes are found in the LSA protein. However, the application neither specifically identifies such epitopes in the regions of residues 1-153, or in other regions of the LSA protein.

It is recognized that there are motifs useful in the identification of the epitopes. However, the knowledge in the art of such motifs does not permit certain identification of the epitopes. This lack of certainty in the identification of epitopes is demonstrated by the teachings of Sette et

al., U.S. 6,689,363. This reference indicates that potential epitopes may be identified through the presence of a sequence motif, but also that additional screening of such peptides is required to determine if such peptides are in fact epitopes. See e.g., column 13, esp. lines 20-23. Thus, in addition to the lack of any specific identification of LSA epitopes in the application, there is also uncertainty in the art regarding the identification of such epitopes.

Moreover, while it is recognized that methods for screening such epitopes are known, the presence of such methods does not provide descriptive support for the epitopes that may be so identified. See e.g., *University of Rochester v. G.D. Searle & Co.*, 69 U.S.P.Q.2d 1886 at 1895 (indicating that the presence of a method for the identification of compounds does not disclose which compounds would have the desired activity being screened for). In view this, and the lack of any sufficient written description support for the epitopes themselves, the claims are rejected as having insufficient support for the claims as drawn to a genus comprising any T- or B- cell epitope, or any epitope generally, that may be found in the LSA protein; although the application does appear to have support for claims drawn to a DNA encoding the LSA of SEQ ID NO: 38, a polypeptide encoding the first 153 amino acids of that LSA protein, or to the individual repeats in this region. Because the application does not provide adequate descriptive support for the indicated genera of epitopes in the LSA protein, the application also lacks adequate support for the present claims which are drawn to nucleic acids encoding such epitopes.

Claim Rejections - 35 USC § 102

16. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

17. Claims 27, 32, and 35 are rejected under 35 U.S.C. 102(b) as being anticipated by Guerin-Marchand et al. (Nature 329: 164-67- of record in the February 2002 IDS). Claim 27 is drawn to a nucleic acid that encodes a polypeptide including at least one T-cell epitope of the liver-stage specific antigen (LSA) of *P. falciparum*. Claim 32 requires the presence of the first 153 amino acids of SEQ ID NO: 38, or an epitope effective portion thereof. Claim 35 requires that the encoded polypeptides additionally have a B-cell epitope.

Guerin-Marchand teaches a DNA sequence encoding a series of repeats from the LSA protein. Page 166, Figure 4. The encoded sequence includes both a sequence identified as a T-cell epitope by González et al. (Parasite Immunol 22: 501-514, at 505, Table 1-KLQEQQSDL), and a sequence disclosed by Londono et al. (J Immunol 145: 1557-63 at 1559) as binding to anti-LSA antibodies (thus, having a B-cell epitope therein). Because both types of epitopes are present in the sequence of Guerin-Marchand, the reference anticipates the indicated claims.

18. Claims 27, 32, and 35 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. 5,602,031. The claims have been described above. The reference teaches DNAs encoding polypeptides disclosed as inducing the production of anti-LSA antibodies (thereby requiring the presence of B-cell epitopes). See e.g., claim 2. In addition, several of these peptides also include the T-cell epitope disclosed by González et al. (supra). The reference therefore anticipates the indicated claims.

19. Claims 27 and 32 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 88/05785 (of record in the February 2002 IDS- a translation of the disclosure of which is found in U.S. 5,599,542). The claims have been described above.

The WO reference teaches peptides representing repeating sequences of the LSA protein corresponding to fragments of SEQ ID NO: 38. Page 6 (lines 33-34) and page 4 (line 4-defining the X as either Glu or Gly); corresponding to column 3 of the patent, and column 2 line 30. The WO reference additionally teaches nucleic acids encoding the peptides. Page 10, lines 25-35 (corresponding to column 5 lines 56-64 of the U.S. patent). It is noted that the reference does not appear to teach that the peptides comprise T-cell epitopes. However, González et al. (supra) teaches that the sequence KLQEQQSDL (representing the embodiment wherein the X is Glu- the peptide found in the native form of SEQ ID NO: 2) is a T-cell epitope. Most of the peptides disclosed by the WO reference include this sequence, and therefore inherently include the T-cell epitope. The reference therefore anticipates the indicated claims.

20. Claims 27 and 32 rejected under 35 U.S.C. 102(a) as being anticipated by Zhu et al. (Mol Biochem Parasitol 48:223-26). The claims have been described above. This reference teaches a DNA encoding an LSA antigen. See e.g., pages 224. The sequence disclosed includes the first 153 residues of SEQ ID NO: 38, and the sequences of both the T-cell epitope of González and the B-cell epitope of Londono. The reference therefore anticipates the indicated claims.

It is noted that this reference has a publication date after the date of foreign priority application FR 91 01286. However, the submitted copy of the foreign application is in a foreign

language. Thus, the Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Claim Rejections - 35 USC § 103

21. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

22. Claims 27, 32, and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 88/05785, as applied against claims 27 and 32 above. Claim 37 reads on the DNA of claim 32, wherein the polypeptide is linked to an additional peptide that is not a *P. falciparum* Liver stage antigen.

The teachings of the WO reference have been described above. While the reference teaches a DNA meeting the limitations of claims 27 and 32, the reference does not teach a DNA including additional non-LSA sequences. However, the reference does suggest the making of such fusion proteins, and therefore of the DNAs encoding such. See e.g., page 5 lines 10-25 (corresponding to the paragraphing spanning columns 2-3 of U.S. patent 5,599,542). The reference therefore renders the DNA of claim 37 obvious.

Double Patenting

23. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

24. Claims 27 and 35 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6 of U.S. Patent No. 5,602,031. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the patent anticipate the present claims. See, anticipation rejection over the '031 patent under 102(b) above.

Conclusion

25. No claims are allowed.

26. The following prior art reference is made of record and considered pertinent to applicant's disclosure. However, while relevant they are also not used as a basis for rejection for the stated reasons.

Londono et al. (J Immunol 145: 1557-63- of record in the February 2002 IDS). As indicated above, this reference teaches a peptide comprising a portion of the LSA protein that includes a B-cell epitope. Additionally, the peptide $(NPNA)_4$N-Th2R-LSA_{27} includes both an LSA T-cell epitope (the Gonzalez epitope disclosed above) and a non-LSA

sequence. However, the reference does not teach a DNA encoding such. Thus, the reference is not applied directly as prior art against the present claims.

27. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Z. Lucas
Patent Examiner